

CLAIMS

What is claimed is:

- ✓ 1. A method for diagnosis of one or more single nucleotide polymorphism(s) in NK1R gene in a human, which method comprises determining the sequence of the nucleic acid of the human at one or more positions:
- 2361 in exon 1 as defined by the position in SEQ ID No. 1;
1371 in the promoter element as defined by the position in SEQ ID No.1;
271 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;
10 272 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;
245 in exon 5 as defined by the position in EMBL ACCESSION NO. X 65181;
461 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;
495 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;
600 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;
15 809 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;
and determining the status of the human by reference to polymorphism in NK1R.
2. A method according to claim 1 in which the single nucleotide polymorphism at position 2361 in exon 1 is presence of C and/or T, the single nucleotide polymorphism at position 1371 in the promoter element is presence of A and/or G, the single nucleotide polymorphism at position 271 near exon 3 is presence of G and/or T, the single nucleotide polymorphism at position 272 near exon 3 is presence of A and/or a single base deletion at this position, the single nucleotide polymorphism at position 245 in exon 5 is presence of C and/or a single base deletion at this position, the single nucleotide polymorphism at position 25 461 in the 3' UTR is presence of G and/or C, the single nucleotide polymorphism at position 495 in the 3' UTR is the presence of T and/or a single base insertion of A at this position, single nucleotide polymorphism at position 600 in the 3' UTR is presence of A and/or G, the single nucleotide polymorphism at position 809 in the 3' UTR is presence of C and/or T.
- 30 3. A method as claimed in claim 1 or 2, wherein the region containing the potential polymorphism is amplified by polymerase chain reaction prior to determining the sequence.

4. A method as claimed in any of claims 1 - 3, wherein the presence or absence of the polymorphism is detected by reference to the loss or gain of, optionally engineered, sites recognised by restriction enzymes.
5. A method according to claim 1 or claim 2, in which the sequence is determined by a method selected from ARMS-allele specific amplification, allele specific hybridisation, oligonucleotide ligation assay and restriction fragment length polymorphism (RFLP).
6. A method as claimed in any of the preceding claims for use in assessing the predisposition and/or susceptibility of an individual to diseases mediated by NK1R ligands.
- ✓ 7. A nucleic acid comprising any one of the following polymorphism containing sequences:
- the nucleic acid sequence of SEQ ID No. 1 with T at position 2361 in exon 1 as defined by the position in SEQ ID No. 1;
 - the nucleic acid sequence of EMBL ACCESSION NO. X 65179 with T at position 271 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;
 - the nucleic acid sequence of EMBL ACCESSION NO. X 65179 with a single base deletion at position 272 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;
 - the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with a single base deletion at position 245 in exon 5 as defined by the position in EMBL ACCESSION NO. X 65181;
 - the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with C at position 461 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181;
 - the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with A inserted at position 495 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181;
 - the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with G at position 600 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181;
 - the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with T at position 809 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181;
 - the nucleic acid sequence of SEQ ID No. 1 with G at position 1371 in the promoter element as defined by the position in SEQ ID No. 1;

or a complementary strand thereof or a fragment thereof of at least 20 bases comprising at least one of the polymorphisms.

- ✓ 8. A diagnostic nucleic acid primer capable of detecting a polymorphism in the NK1R gene at one or more of positions: 2361 in exon 1 as defined by the position SEQ ID No. 1; 1371 in the promoter element as defined by the position SEQ ID No. 1; 271 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179; 272 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179; 245 in exon 5 as defined by the position in EMBL ACCESSION NO. X 65181; 461 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181; 495 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181; 600 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181; 809 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181, in the NR1R gene.
- 15 9. A diagnostic primer as claimed in claim 8 which is an allele specific primer adapted for use in ARMS.
- ✓ 10. An allele-specific oligonucleotide probe capable of detecting a polymorphism in the NK1R gene at one or more of positions: 2361 in exon 1 as defined by the position in SEQ ID No. 1; 1371 in the promoter element as defined by the position in SEQ ID No. 1; 271 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179; 272 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179; 245 in exon 5 as defined by the position in EMBL ACCESSION NO. X 65181; 461 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181; 495 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181; 600 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181; 809 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181, in the NR1R gene.
- 25 11. A diagnostic kit comprising one or more diagnostic primer(s) as defined in claim 8 or 9 and/or one or more allele-specific oligonucleotide probes(s) as defined in claim 10.
- 30

✓ 12. An allelic variant of human NK1R polypeptide having a C-terminal deletion of 26 amino acids.

✓ 13. A method of treating a human in need of treatment with an NK1R ligand antagonist
5 drug in which the method comprises:

(i) diagnosis of a single nucleotide polymorphism in the NK1R gene in the human, which diagnosis comprises determining the sequence of nucleic acid at one of more of positions:

2361 in exon 1 as defined by the position SEQ ID No. 1;

1371 in the promoter element as defined by the position in SEQ ID No. 1;

10 271 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;

272 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;

245 in exon 5 as defined by the position in EMBL ACCESSION NO. X 65181;

461 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;

495 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;

15 600 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;

809 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;

and determining the status of the human by reference to polymorphism in the NK1R gene;

and

(ii) administering an effective amount of a NK1R ligand antagonist.

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✓ 14. Use of an NK1R ligand antagonist drug in preparation of a medicament for treating a NK1R ligand mediated disease, particularly asthma, in a human diagnosed as having a single nucleotide polymorphism at one or more of positions:

2361 in exon 1 as defined by the position in SEQ ID No. 1;

25 1371 in the promoter element as defined by the position in SEQ ID No. 1;

271 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;

272 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;

245 in exon 5 as defined by the position in EMBL ACCESSION NO. X 65181;

461 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;

30 495 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;

600 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;

809 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181.

- ✓ 15. A pharmaceutical pack comprising an NK1R antagonist drug and instructions for administration of the drug to humans diagnostically tested for a single nucleotide polymorphism at one or more positions:
2361 in exon 1 as defined by the position in SEQ ID No. 1;
5 1371 in the promoter element as defined by the position in SEQ ID No. 1;
271 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;
272 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;
245 in exon 5 as defined by the position in EMBL ACCESSION NO. X 65181;
461 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;
10 495 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;
600 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;
809 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181.
- ✓ 16. A computer readable medium having stored thereon a member selected from the group
15 consisting of: a nucleic acid comprising SEQ ID No. 1; a set of nucleic acids wherein at least one of said sequences comprises SEQ ID No. 1; a data set representing a nucleic acid sequence comprising SEQ ID No. 1; a nucleic acid consisting of SEQ ID No. 1; a set of nucleic acids wherein at least one of said sequences consists of the sequence of SEQ ID No. 1; a nucleic acid comprising any part of a sequence selected from the group consisting of: SEQ
20 ID No. 1, EMBL ACCESSION NO. X 65177, EMBL ACCESSION NO. X 65179, EMBL ACCESSION NO. X 65179 or EMBL ACCESSION NO. X 65181, which part includes at least one of the polymorphisms identified in claim 1.
- ✓ 17. A method for performing sequence identification, said method comprising the steps of
25 providing a nucleic acid sequence comprising a sequence selected from the group consisting of: the nucleic acid sequence of SEQ ID No. 1 with T at position 2361 in exon 1 as defined by the position in SEQ ID No. 1; the nucleic acid sequence of EMBL ACCESSION NO. X 65179 with T at position 271 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179; the nucleic acid sequence of EMBL ACCESSION NO. X 65179 with a single
30 base deletion at position 272 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with a single base deletion at position 245 in exon 5 as defined by the position in EMBL ACCESSION NO.

X 65181; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with C at position 461 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with A inserted at position 495 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with G at position 600 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with T at position 809 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181; the nucleic acid sequence of SEQ ID No. 1 with G at position 1371 in the promoter element as defined by the position in SEQ ID No. 1; or a complementary strand thereof or a fragment thereof of at least 20 bases comprising at least one of the polymorphisms; and comparing said nucleic acid sequence to at least one other nucleic acid or polypeptide sequence to identify identity.

18. A method for performing sequence identification, said method comprising the steps of providing one or more of the following polymorphism containing nucleic acid sequences: the nucleic acid sequence of SEQ ID No. 1 with T at position 2361 in exon 1 as defined by the position in SEQ ID No. 1; the nucleic acid sequence of EMBL ACCESSION NO. X 65179 with T at position 271 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179; the nucleic acid sequence of EMBL ACCESSION NO. X 65179 with a single base deletion at position 272 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with a single base deletion at position 245 in exon 5 as defined by the position in EMBL ACCESSION NO. X 65181; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with C at position 461 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with A inserted at position 495 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with G at position 600 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with T at position 809 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181; the nucleic acid sequence of SEQ ID No. 1 with G at position 1371 in the promoter element as defined by the position in SEQ ID No. 1; or a complementary strand thereof or a fragment thereof of at least 20 bases comprising at

least one of the polymorphisms, in a computer readable medium; and comparing said nucleic acid sequence to at least one other nucleic acid or polypeptide sequence to determine identity.

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Year	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100
1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	